Carbohydrates

Today we will talk about carbohydrates, metabolism (digestion, absorption, and transport the carbohydrates)

*SLIDE (1):

- This slide shows the *Dietary carbohydrates* that need digestion
- The carbohydrates are digestible
- The carbohydrates almost constitute 50% of the calories consumed by humans
- Most of carbohydrates are complex carbohydrates in the form of amylase and amylopectin, which are found in grains, potatoes, rice, and vegetables (are the main source of carbohydrates)
- Carbohydrates can be either polysaccharide (complex molecule) or they can be disaccharide
- Examples of polysaccharide:
  - Amylose: is polymer of glucose in alpha (1-4) glycosidic linkage that is unbranched and non-helical straight chain (not stright). The importance of it is to store glucose for plants, and we use it as a source of food (calories)
  - Amylopectin: is polymer of alpha (1-4) glucose in each (10-15) residue, there is a branch in this branching point
• Amylose and Amylopectine are found in the starch
• Examples of disaccharide:
  • Sucrose:

  - that is found in vegetables, fruits, and

  - All sugar is constituent a lot of calories for the body

  - it is formed from: glucose and fructose, they are connected by glycosidic bond of C1 of glucose with C2 of fructose, alpha (1-2)

  - the sugar food from animal origin is:

    * LACTOSE

    - Which found in milk.

    - is formed from: glucose and galactose

    - the glycosidic linkage is: beta (1-2) C1 of galactose with C2 of glucose

*** In addition to these, there are monosaccharides that do not need digestion:

Glucose and fructose which found in some food like honey and fruit

*SLIDE (2):

* The aim of digestion is to covert polysaccharide and disaccharide to monosaccharide by breaking the
glycosidic linkage between sugar residues, this is catalyzed by **glycosidase** which hydrolyze the bond by addition of water

*The bond which connect the sugar residues together called **glycosidic** bond which is between C1 (ANOMERIC C) and any hydroxyl group (OH)

*In any sugar:

- C1 is linked to OXYGEN
- it has different ends (not symmetric)

1-REDUCING END

2-NON REDUCING END: it has (OH) on C4

-Sugar can be alpha or beta

1-ALPHA: if oxygen is below the ring

2-BETA: if oxygen is above the ring

***The glycosidases differ in their **specificity** with regard to type of sugar and type of glycosidic bond, it is not one type of glycosidases there are many type of glycosidases that differ in their specificity (which sugar they can beta glycosidic bond)

**SLIDE (3):**

The enzymes that we are going to give it:
• **Alpha Amylase:**

-it found in salivary, and disaccharidases (in the intestine).

*NOTE:*

-Not all carbohydrates are digested by human enzymes, some of them like **CELLULOSE** cannot be digested by human enzymes (because it is beta, and it is no specific enzymes for cleaving beta bond).

-These dietary carbohydrates not necessary to contribute to calories intake, they help in absorption of water because they are hydrophilic so they facilitate the transport of food in the small and large intestine and some of them are digested by **c-THE DIGESTION PROCESS: colonic bacteria** (bacteria which is found in the colon)

***Human enzymes cannot digest the fiber carbohydrates***

*SLIDE (4):*

1-During the MASTICATION the food that we eat (starch, lactose, sucrose, and cellulose), the **salivary gland** secrete an AMYLASE, which is the major enzyme in saliva.
Note:

-the salivary gland secrete 1000 ml of saliva, the major enzymes of this saliva, is ALPHA AMYLASE

2- Alpha Amylase begin acting in the mouth during chewing of food but it rapidly will be inactivated when the food reach the stomach because of low PH (1-1.5) which stop the action of salivary amylase because of denaturation so the importance of it: to get rid of any food remain in the mouth.

3- Then the food enters the small intestine in the Duodenum.

4- Then it enter the Pancreas that secrete its secretion (Pancreatic juice which rich in bicarbohydrates that neutralize the acid content of the stomach) so the pancreatic amylase that is similar to salivary amylase will continue the work by cutting the carbohydrates or amino peptide into small pieces.

*Note:

- Alpha Amylase also works in alkaline media.

- Alpha Amylase cannot digest the isomaltose, maltose, lactose, and sucrose. But they are digested by enzymes that are found in small intestine.
5- The mucosal cell membrane-bound enzymes convert the isomaltase, maltase, lactase, and sucrose into glucose, fructose, and galactose.

6- Then these products will be absorbed through portal circulation to reach the liver.

*SLIDE (5):

- This is a chain of starch connected by alpha (1-4)glycosidic linkage but at the branching point the glycosidic linkage is alpha (1-6).

- It has two kinds of different ends (reducing and non-reducing end) but in this case, it has one reducing end and many non-reducing ends.

- The salivary amylase can cut this chain of starch randomly so this process produces different products (it may be produce maltose or isomaltose or dextrin depend on "how the salivary amylase cut the starch").

*SLIDE (6):  

- This is a part of glycogen molecule

- glycogen has similar structure to the amylopectin, but glycogen is more branched.

- By cleavage of alpha (1-4), then the glycogen produce the maltose and maltotriose.
- By cleavage of alpha (1-6) glycosidic linkage, then the glycogen produce oligosaccharide.

*SLIDE (7):

- The disaccharidases are found in the intestinal brush border which full of villi which have absorptive cells, the aim of these cells is to increase the surface area and to facilitate the digestion and absorption.

- The disaccharidases attach to the membrane of brush border (they are produced by the cells but they are not excretion, they do not leave the cell, they remain attach to the membrane of brush border).

- We have 4 types of enzymes:

  1- Glucoamylase.

  2- Sucrase isomaltase.

  3- Beta glycosidase.

  4- Trehalase.

- These enzymes are found in Jejunum, and they have different distribution but they mostly found in jejunum.

- The concentration of glucoamylase increase until it reach to the ilium so the amount of enzymes in the intestine increase as we go down, but the maximum
concentration of glucomylase is found in jejunum in the case of sucrose.

*SLIDE (8):

-GLUCOAMYLASE:

-is oligosaccharide and heavily glycosylated (full of sugar residues which protect the enzymes, that are found on the extracellular surface, from many proteases, digestion enzymes, and trypsin (or from degradation).

-It is similar structure to SUCRASE ISOMALTASE.

-It has 2 domain with similar activity.

-Glycoamylase is Exoglcosidase (opposite to endoglucosidase).

-This exoglcosidase act on the non reducing end.

*Note:

-If it acts only on "reducing end", there will be only one end per molecule.

-But it acts on "non reducing end", so there are large number like in the case of dextrins.

-Exoglcosidase means it remove one glucose.

-The dextrins convert to isomaltose by this enzyme.
GLUCOAMYLASE ACTIVITY

- once the bond is cleaved by glucoamylase then the bonds will be cleaved by maltase activity.

SUCRASE ISOMALTASE COMPLEX STRUCTURE

- It is similar to glucoamylase
- It is attached to the membrane.
- It has 2 domain (sucrose domain and isomaltase domain).
- It has connecting segment (stalk).
- It has carbohydrates chain which protect from protease action.
- It is hydrated so the enzymes protrude on the membrane.
- It expose the protein and enzymes inside the lumen of the small intestine.

(SUCRASE-ISOMALTASE COMPLEX) is 2 proteins because it has C-terminal and N-terminal.
**Actually it synthesize as one protein but it cleaved .but even it cleaved ,it remain attach to each other by "non covalent interaction".

- Each subunit (sucrose-maltase domain and isomaltase-maltase domain ) has maltase activity .

- Both of them will hydrolyze maltose as well.

**Slide 11**

Beta-glycosidase complex is a protein complex that hydrolyze the carbon-carbon beta-glycosidic bond it's a large glycolprotein attached to the brush border ,it hydrolyzes lactose ,which is a galactose binding to glucose via beta-glycosidic bond .**this bond is hydrolyzed by beta-glycosidase**

So this enzyme catalyzes the hydrolysis of terminal non reducing beta-galactose residues in lactose

**Remember that glyco means ;sugar ,and this enzyme recognize the beta-glycosidic bond between galactose and glucose**

This enzyme has two catalytic sites (two subunits), means they are not similar.
The first subunit is called lactase; which has lactase activity (hydrolysis of lactose as we mentioned before). And the other subunit is called glucosylceramidase.

**A Brief explanation**

Ceramide is a sphingolipid consist of a sphingosine backbone attached to one fatty acid group, while cerebroside is a glycolipid contains ceramide and sugar residues, the sugar is either glucose or galactose.

So this enzyme (glucosylceramidase), hydrolyzes ceramide attached to glucose or galactose, (hydrolyzes cerebrosides), breaking the bond between ceramide and sugar.

**Slide 12&13&14**

Lactose intolerance;

Lactose is ingested from the food, and it founds principally in milk and their products, lactase is an enzyme that digest lactose, which found in milk, but lactase level in the intestine start to decrease from the first month of age, so usually during the normal process, level of lactase stay increasing during the late gestation until the baby reaches the first month of his age, and then start to decrease.
So the lactose intolerance due to lactase deficiency will lead to pain (abdominal pain), nausea, flatulence.

**Most of the population are non-persistent lactase, the adult level reaches 10% of the infant level at 5-7 age; means that people who are between 5-7 years old will have just 10% of the original level of lactase, this case roughly meets half of the world.**

Asia world suffer from lactase deficiency, while Europe; west Europe, like Holland, the lactase level remains until the adulthood in high levels.

The ingestion of lactose in milk for old people, will lead to severe pain (abdominal pain), nausea and flatulence.

**People, who has lactase deficiency, the lactose**

![Diagram](image-url)
galactose, so it will pass all the route to the large intestine, because the absorption of lactose in small intestine doesn't occur, now in the large intestine, lactose will meet the bacteria of the large intestine, this bacteria utilize lactose and cause fermentation.

The fermentation will lead to the production of different metabolites, which are:

2-carbon metabolites (such as: acetic acid), 3-carbon metabolites (such as: lactic acid), CO2, H2, in brief the products are a combination of gases.

Why diarrhea occurs in lactase deficiency people?

As we mentioned before lactose doesn't undergo digestion and absorption, so it moves to the large intestine and is subjected to fermentation by bacteria, however all the products are small molecules (except hydrogen), means they have a large osmotic pressure, and water level inside intestine will be low in comparison to metabolites, consequently, water will move from interstitial fluid to the intestine, and this will increase the level of water in the large intestine, the loss of that water will be by diarrhea, and this will lead to dehydration.
10% of lactase level in adults is enough for drinking one cup of milk, but if you want to drink 10 cups, you will enjoy the pain (severe abdominal pain), and you will have the chance for going to the hospital (if you are not from European people)

One glass of milk is about 200 ml, will resulted in loss of one liter of extracellular fluid (water), dehydration occurs, and a lot of fluid will lost by lactase deficiency

Lactase deficiency might occur due diseases; any disease that affect or cause injury to small intestinal cells, will lead to lactase, sucrose and isomaltase deficiencies.

All these disaccharidases will be affected and will be lost from the small intestine. The most enzyme by which affected is lactase, while the others (other disaccharidases) can be affected in a transient form, which means they recover rapidly.
Absorption of sugars:

Sugars are highly polar molecules, so they can easily bind to H2O by H bonds. These hydrophilic molecules (sugars which are hydrated by H2O), will pass the lipid by layer with the help of transporters; so there must be transporters in the small intestine during the process of absorption.

To carry this highly polar molecules across the hydrophobic membrane into the cell, transport protein are needed.

The transport of sugars across membrane is achieved by two different mechanism, which are:

** Active transport: there is a transporter called NA+ dependent glucose transporter, this type of transport requires energy (ATP).

** Facilitated transporter, which is facilitated glucose transporters.

Two types of transporter are specific for absorption of sugars across the intestinal cells

Study the picture that follows;
Look at the absorptive cell, that has the brush border on its apical side, notice the sodium/dependent glucose transporter.

**How this transporter works??**

The concentration of glucose in the lumen of small intestine is low, and its concentration inside the cells of the intestine is high; the glucose must pass from the low to the high concentration, so how can we transport a substance against its concentration gradient???

It needs energy, in our example we use energy indirectly

By making the sugar; which is glucose in our example
co-transported with a substance that is found in high concentration in the lumen of the small intestine.

Sodium has this property, it transport down its concentration gradient (from high to low concentration)

Although the transport of sodium doesn't need energy, this type of transporter will not allow sodium to be transported unless the glucose is transported as well.

Once the sodium binds, and glucose binds too, \( \text{Na}^+ \) and glucose will be transported across the membrane, and ultimately they will be inside the intestinal cell.

What makes sodium concentration low in the intestinal cells??

By the help of sodium/potassium ATPase, which pumps sodium outside the cell (3 \( \text{Na}^+ \) at a time)

Galactose as glucose, uses the same transporter (\( \text{Na}^+ /\text{Glucose co transporters} \))

***when glucose or galactose enters the intestinal cell, their concentration will be higher than the blood (capillaries), so the sugar will be transported by
facilitated diffusion across the serosal side from the cells to capillaries (high to low concentration),

Glucose can be also transported to the intestine and out of the intestine (as we mentioned in the previous paragraph) by facilitative diffusion.

When glucose is found in high concentration in the lumen, it will use this property to transport across membrane via facilitative transporters, where we don't need energy, and as we mentioned before it can transported across the serosal side going to the blood by the same way.

Clinical Application

Before discovering the sodium / glucose dependent transporter, when small babies are suffered from diarrhea and dehydration, doctors were giving an intravenous rehydration solution, (in the past they thought that sodium can't pass the intestinal cell).

After discovering the transporter that pass the NA+ and glucose together they found that if you give the baby a solution that contains both sodium chloride and glucose, the absorption of sodium will occur (because of the transporter; NA+/Glucose dependent transporter), and rehydration.

If you give to the patient just a solution of salt and water, sodium will not be transported, why?????

*because sodium can't enter the cell without being co-transported with glucose.
Doctors tend now to treat dehydration and diarrhea by giving an oral rehydration that is available in pharmacies, by this way patients can compensate for the body loss of fluids.

**Facilitative transport of glucose:**

The proteins that mediate the transport of glucose by facilitated transport, found in the membrane as integral proteins, they possess outside and inside parts.

**Mechanism of working:**

glucose can bind to the transporter, because it's opened from its outside parts (the side toward the lumen), once glucose bind, this will cause a conformational change in the transporter in a way that it will close from outside and open from the other side.

In the opposite side the glucose level is low, so it dissociates (transported to capillaries).

Glucose transported from the outside to inside, or from the inside to the outside depending on the concentration (from high to low).

*from outside to inside: from the lumen to cell*

*from inside to outside: from cell to capillary*

The facilitative transporters are a family of similar proteins, have 12 membrane spanning domains, they are not one protein, but number of proteins reach 14.
The most important are 5; they called GLUT (Glucose transporter).

SLIDE (18):
*Please refer to the slide, the doctor read it all ,I want to write the extra information related to it .

*We have numbers of protein which called (glucose transporter) ,the most famous families are GLUT(1,2,3,4,5).

*KM of enzyme: the concentration that is needed to produce half of the maximum velocity.
- e.g.: the concentration of substrate (glucose) that cause 50% of the transporter to be occupied =1 ml .
- The normal concentration of glucose is (five times of KM)=5 ml.

*The transporter work in full capacity.
*GLUT 1 is found in certain barrier function like in brain.

*As you notice, that in the liver there is GLUT 2  which the KM=15 (high KM), why ?????...

-when the glucose in the blood is high after food intake , it is important to transfer glucose inside the liver so it is active only when the concentration of glucose in the blood is high .
*beta pancreatic (beta cells) is glucose sensor

-when glucose is enter to the beta cells of pancreatic which is found in high concentration so the pancreatic cell know that the blood glucose is high so it should secrete the insulin.

*You notice that KM of GLUT 4 is 5 ml (low affinity) why???...

- because the glucose transporters dependent on insulin when insulin level increase, the amount of GLUT 4 is increase.

-Glucose enter to adipose cells and muscles in only case , when the glucose is found in high level.

*increase in glucose so the insulin is high (this is sensitive to presence of insulin).

**SLIDE (19)**

STAIMULATION OF GLUCOSE TRANSPORT INTO MUSCLE AND ADIPOSE CELLS BY **Insulin**.

**when insulin level is high so it is bind to its receptors through number of events** .

**GLUT are transported from vesicles (the initial), then it will be inserted to the membrane.**
**when the insulin decrease, they will be recycled again and they go to the GLUT vesicles and they aggregate in the cytosol.**

SLIDE (20)

*The doctor read exactly what we have in the slide.*

BEST WISHES......

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